

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-19 (canceled)

Claim 20 (currently amended) A method for administering a biologically active agent, the method comprising:

injecting a formulation comprising:

(a) an injection vehicle comprising hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight per volume; and

(b) particles comprising:

- (i) a first component that is the biologically active agent; and
- (ii) a second component that is a biocompatible polymeric matrix,

wherein the concentration of the particles is about 100 mg/mL to about 500 mg/mL of the formulation,

and further wherein the hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is at a concentration sufficient to inject the formulation through a 23-gauge or smaller bore needle.

Claim 21 (canceled)

Claim 22 (currently amended) An injectable formulation, comprising:

(a) an injection vehicle comprising hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate dissolved in a physiological buffer at a concentration of about 0.01 to about 3 percent weight by volume; and

(b) particles, comprising:

- (i) a first component that is a biologically active agent, and
- (ii) a second component that is a biocompatible polymeric matrix,

wherein the concentration of the particles is about 100 mg/mL to about 500 mg/mL of the formulation,

and further wherein the hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is at a concentration sufficient to inject the particles through a 23-gauge or smaller bore needle.

Claim 23 (previously presented) The injectable formulation of claim 22, wherein the physiological buffer comprises physiological saline.

Claim 24 (canceled)

Claim 25 (previously presented) The injectable formulation of claim 22, wherein the polymeric matrix comprises a blocked polymer.

Claim 26 (previously presented) The injectable formulation of claim 22, wherein the polymeric matrix comprises an unblocked polymer.

Claim 27 (previously presented) The injectable formulation of claim 22, wherein the polymeric matrix comprises poly(lactide-co-glycolide).

Claim 28 (previously presented) The injectable formulation of claim 22, wherein the biologically active agent is a polypeptide.

Claim 29 (previously presented) The injectable formulation of claim 28, wherein the polypeptide is selected from the group consisting of a growth hormone, a cytokine; a cytokine receptor; a chimeric protein comprising a cytokine or its receptor; a tumor necrosis factor; a tumor necrosis factor receptor; a tumor necrosis factor derivative; a lipoprotein; a clotting factor; an anti-clotting factor; a serum albumin; a microbial protein; a receptor for a hormone; a receptor for a growth factor; a rheumatoid factor; a neurotrophic factor; a nerve growth factor; a fibroblast growth factor; a transforming growth factor (TGF); a CD protein; an osteoinductive factor; an immunotoxin; a bone morphogenetic protein (BMP); an interferon; a colony stimulating factor (CSF); an interleukin (IL); a viral antigen; a transport protein; a homing receptor; a regulatory protein; an antibody; a portion of an antibody; a chimeric protein, a plasminogen activator; a tissue-type plasminogen activator; a urokinase; an insulin-like growth factor binding protein; a T-cell

receptor; a surface membrane protein; an HIV-1 envelope glycoprotein; a fragment of gp120; a fragment of gp160; a Fab fragment; and an immunoadhesin.

Claim 30 (canceled)

Claim 31 (previously presented) The injectable formulation of claim 22, wherein the concentration of the particles in the formulation is about 1 100 mg/mL to about 300 mg/mL.

Claim 32 (canceled)

Claim 33 (currently amended) The injectable formulation of claim 22, wherein the ~~hyaluronic acid derivative is N-acylurea modified injection vehicle comprises~~ hyaluronic acid.

Claim 34 (currently amended) The injectable formulation of claim 22, wherein the ~~hyaluronic acid derivative is injection vehicle comprises~~ sodium hyaluronate.

Claim 35 (canceled)

Claim 36 (previously presented) The injectable formulation of claim 28, wherein the polypeptide is an anti-vascular endothelial growth factor Fab (anti-VEGF Fab).

Claim 37-39 (canceled)

Claim 40 (currently amended) The method of claim 20, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is about 0.01 to about 1 percent weight per volume.

Claim 41 (currently amended) The method of claim 40, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is about 0.01 to about 0.8 percent weight per volume.

Claim 42 (currently amended) The injectable formulation of claim 22, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is about 0.01 to about 1 percent weight per volume.

Claim 43 (currently amended) The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is about 0.01 to about 0.8 percent weight per volume.

Claim 44 (canceled)

Claim 45 (previously presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from a biodegradable polymer, a non-biodegradable polymer, a mixture of biodegradable and non-biodegradable polymers, and a copolymer comprising biodegradable and non-biodegradable units.

Claim 46 (previously presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from blocked polymers, unblocked polymers, and mixtures of blocked and unblocked polymers.

Claim 47 (previously presented): The injectable formulation of claim 22, wherein the polymeric matrix comprises a polymer selected from a poly (glycolide); a poly (lactide-co-glycolide); a poly (lactic acid); a poly (glycolic acid); a poly (lactic acid- co-glycolic acid); a polyanhydride; a polyorthoester; a polyetherester; a polycaprolactone; a polyesteramide; a block copolymer of polyethylene glycol and lactide; a block copolymer of polyethylene glycol and glycolide; and blends or copolymers thereof.

Claim 48 (currently amended): A method for making a pharmaceutical formulation, comprising:

adding an effective amount of a biologically active agent coated on, dispersed within, or coated on and dispersed within polymeric particles to an aqueous injection vehicle comprising hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate at a concentration of about 0.01 to about 3% (w/v);

wherein the concentration of particles in the formulation is between about 100 and 500 mg/mL (w/v); and further wherein the hyaluronic acid or ~~a derivative thereof~~ sodium

hyaluronate is at a concentration sufficient to inject the particles through a 23-gauge or smaller bore needle.

Claim 49 (currently amended): A method for administering ~~a pharmaceutical~~ the injectable formulation of claim [[20]] 22, comprising: injecting the ~~pharmaceutical~~ injectable formulation through a 23-gauge or smaller bore needle.

Claim 50 (previously presented): The injectable formulation of claim 22, wherein the biologically active agent is dispersed within, coated on, or dispersed within and coated on the particles.

Claim 51 (previously presented): The injectable formulation of claim 50, wherein the biologically active agent is dispersed within the particles.

Claim 52 (previously presented): The injectable formulation of claim 22, wherein the particles are microparticles.

Claim 53 (previously presented): The injectable formulation of claim 22, wherein the particles are microspheres.

Claim 54 (previously presented): The injectable formulation of claim 22, wherein the particles have an average diameter of between about 5 and about 200 microns.

Claim 55 (currently amended): The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is between about 0.05 and about 1 percent weight per volume.

Claim 56 (currently amended): The injectable formulation of claim 42, wherein the concentration of hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is between about 0.05 and about 0.8 percent weight per volume.

Claim 57 (previously presented): The injectable formulation of claim 22, wherein the concentration of particles in the formulation is between about 125 mg/mL to about 250 mg/mL.

Claim 58 (previously presented): The injectable formulation of claim 22, wherein the concentration of particles in the formulation is between about 200 mg/mL to about 250 mg/mL.

Claim 59 (previously presented): The injectable formulation of claim 28, wherein the polypeptide is selected from the group consisting of tumor necrosis factor-alpha (TNF-alpha); tumor necrosis factor-beta (TNF-beta); tumor necrosis factor receptor-1 (TNFR-1); tumor necrosis factor receptor-2 (TNFR-2); renin; human growth hormone; bovine growth hormone; growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; alpha-1-antitrypsin; insulin A-chain; insulin B-chain; proinsulin; follicle stimulating hormone; calcitonin; luteinizing hormone; glucagon; factor VIIIC; factor IX; tissue factor; von Willebrand's factor; Protein C; atrial natriuretic factor; lung surfactant; bombesin; thrombin; hemopoietic growth factor; enkephalinase; RANTES; human macrophage inflammatory protein (MIP-1-alpha); human serum albumin; mullerian-inhibiting substance; relaxin A-chain; relaxin B-chain; prorelaxin; mouse gonadotropin-associated peptide; beta-lactamase; DNase; inhibin; activin; vascular endothelial growth factor (VEGF); anti-VEGF Fab; glucagon-like peptide I (GLP-I); hepatocyte growth factor (HGF); integrin; protein A; protein D; bone-derived neurotrophic factor (BDNF); neurotrophin-3, -4, -5, and -6 (NT-3, NT-4, NT-5, NT-6); NGF-beta; platelet-derived growth factor (PDGF); aFGF; bFGF; epidermal growth factor (EGF); TGF-alpha; TGF-beta, including TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta4, and TGF-beta5; insulin-like growth factor-I (IGF-I); insulin-like growth factor-II (IGF-II); des (1-3)-IGF-I (brain IGF-I); CD-3; CD-4; CD-8; CD-19; erythropoietin; interferon-alpha; interferon-beta; interferon-gamma; M-CSF; GM-CSF; G-CSF; IL-1; IL-2; IL-3; IL-4; IL-5; IL-6; IL-7; IL-8; IL-9; IL-10; superoxide dismutase; decay accelerating factor; gp120; gp160; and addressin.

Claim 60 (previously presented): The method of claim 20, wherein the injection vehicle comprises hyaluronic acid.

Claim 61 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 24-gauge needle.

Claim 62 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 25-gauge needle.

Claim 63 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 26-gauge needle.

Claim 64 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 27-gauge needle.

Claim 65 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 28-gauge needle.

Claim 66 (currently amended): The method of claim 20, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 30-gauge needle.

Claim 67 (canceled):

Claim 68 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 24-gauge needle.

Claim 69 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 25-gauge needle.

Claim 70 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or a derivative thereof sodium hyaluronate is at a concentration sufficient to inject the formulation through a 26-gauge needle.

Claim 71 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is at a concentration sufficient to inject the formulation through a 27-gauge needle.

Claim 72 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is at a concentration sufficient to inject the formulation through a 28-gauge needle.

Claim 73 (currently amended): The injectable formulation of claim 22, wherein the hyaluronic acid or ~~a derivative thereof~~ sodium hyaluronate is at a concentration sufficient to inject the formulation through a 30-gauge needle.